CLAIMS

We claim:

- 1. A method for treating a fluid to neutralize microorganisms which may be present therein, said fluid containing one or more components selected from the group consisting of protein, blood, and blood constituents, said method comprising:
 - (a) adding to said fluid a neutralization-effective amount of a microorganism neutralizer of formula:

wherein R1, R2, R3, R4, R5 and R6 are, independently from one another, selected from the group consisting of hydrogen; -OH; NH₂; -SO₄; -PO₄; -Cl; -Br; -I; optionally substituted alkyl, alkenyl, alkynyl or aryl groups with from 1 to 20 carbon atoms; straight chain or cyclic saccharides with 5 or 6 carbon atoms;

$$\begin{array}{c|c} \text{OH} \\ -\text{C} - \text{CH}_2\text{O-} \\ \text{H} \\ \text{HO} & \text{OH} \end{array}$$

and amino acid groups; said groups optionally substituted with one or more of -O-, -S-, -OH, -NH $_2$, -SO $_4$, -PO $_4$, -Cl, -Br, and -I; and

-NR^a-(CR^bR^c)_n-X wherein X is a halogen selected from the group consisting of chlorine, bromine and iodine, R^a, R^b and R^c are, independently of each other, selected from the group consisting of hydrogen, optionally substituted alkyl, alkenyl, alkynyl or aryl groups

with from 1 to 20 carbon atoms; straight chain or cyclic saccharides with 5 or 6 carbon atoms;

and amino acid groups; said groups optionally substituted with one or more of -O-, -S-, -OH, -NH $_2$, -SO $_4$, -PO $_4$, -Cl, -Br, -I; salts of the foregoing; and halogen selected from the group consisting of chlorine, bromine and iodine, and n is an integer from 0 to 20;

provided that R1 is neither H nor -OH nor a straight chain alkyl group where the second carbon of the chain is substituted with -OH or =O and R1, R4, R5 are not all methyl groups when R2, R3 and R6 are hydrogen; except that the compound may be

or

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and provided that the neutralizer is not:

wherein X is a halogen selected from the group consisting of chlorine, bromine and iodine, R^a, R^b and R^c are, independently of each other, selected from the group consisting of hydrogen, optionally substituted hydrocarbyl, and halogen selected from the group consisting of chlorine, bromine and iodine, and n is an integer from 0 to 20; and provided that the neutralizer is not:

wherein W is a water soluble group; and

(b) exposing the fluid of step (a) to a triggering event whereby said microorganisms are neutralized.

2. The method of claim 1, wherein R1, R2, R3, R4, R5 and R6 are, independently from one another, selected from the group consisting of hydrogen; straight chain or cyclic saccharides with 5 or 6 carbon atoms; amino acid groups; -NH₂;-SO₄; -PO₄; -Cl; -Br;-I;

and alkyl, alkenyl, alkynyl or aryl groups with from 1 to 20 carbon atoms containing one or more members selected from the group consisting of: -O-,-C(=O), -C(=O)H, -C(=O)-OH, -OH, -NH₂,-SO₄, -PO₄, -Cl, -Br, and -I.

- 3. The method of claim 1, wherein said triggering event is photoradiation sufficient to activate the microorganism neutralizer.
- 4. The method of claim 1, wherein said triggering event is a pH sufficient to activate the microorganism neutralizer.
- 5. The method of claim 4, wherein said pH is between about 5 and about 8.
- 6. The method of claim 1 wherein said microorganisms are selected from the group consisting of bacteria, bacteriophages, and intracellular and extracellular viruses.
- The method of claim 1 wherein said microorganisms are bacteria.
 - 8. The method of claim 1, wherein said microorganisms are selected from the group consisting of HIV viruses, hepatitis viruses, sindbis virus, cytomegalovirus, vesicular stomatitis virus, herpes simplex viruses, vaccinia virus, human T-lymphotropic retroviruses, HTLV-III, lymphadenopahy virus LAV/IDAV, parvovirus, transfusion-

transmitted (TT) virus, Epstein-Barr virus, bacteriophages Φ X174, Φ 6, λ , R17, T_4 , T_2 , P. aeruginosa, S. aureus, S. epidermidis, L. monocytogenes, E. coli, K. pneumoniae and S. marcescens.

9. The method of claim 1, wherein said microorganism neutralizer is

wherein R is selected from the group consisting of -OH; -NH₂; -SO₄; straight chain or cyclic saccharides with 5 or 6 carbon atoms;

and alkyl, alkenyl, alkynyl or aryl groups with from 1 to 20 carbon atoms containing one or more members selected from the group consisting of: -O-, -SO₄, -PO₄,-OH and -NH₂.

- 10. The method of claim 1, wherein said fluid comprises blood constituents.
- 10 11. The method of claim 1, wherein said fluid comprises whole blood.
 - 12. The method of claim 1, wherein said fluid comprises a separated blood product.
 - 13. The method of claim 1, wherein said fluid comprises platelets separated from whole blood.

- 14. The method of claim 1, wherein said fluid comprises red blood cells separated from whole blood.
- 15. The method of claim 1, wherein said fluid comprises serum separated from whole blood.
- 16. The method of claim 1, wherein said fluid comprises plasma separated from whole blood.
- 5 17. The method of claim 1, wherein said fluid comprises a therapeutic protein composition.
 - 18. The method of claim 1, wherein said fluid contains a biologically-active protein selected from the group consisting of: factor VIII, Von Willebrand factor, factor IX, factor X, factor XI, Hageman factor, prothrombin, anti-thrombin III, fibronectin, plasminogen, plasma protein fraction, peritoneal dialysis solutions, immune serum globulin, modified immune globulin, albumin, plasma growth hormone, somatomedin, plasminogen streptokinase complex, ceruloplasmin, transferrin, haptoglobin, antitrypsin and prekallikrein.
 - 19. The method of claim 1, wherein said microorganism neutralizer is added to anticoagulant and said anticoagulant is added to said fluid.
- The method of claim 1, wherein an enhancer is added to said fluid prior to exposing said fluid to said triggering event.
 - The method of claim 20, wherein said enhancer is selected from the group consisting of adenine, histidine, cysteine, tyrosine, tryptophan, ascorbate, -acetyl-L-cysteine, propyl gallate, glutathione, mercaptopropionylglycine, dithiothreotol, nicotinamide, BHT, BHA, lysine, serine, methionine, glucose, mannitol, trolox, glycerol, and mixtures thereof.

- 22. The method of claim 1, wherein if said microorganism neutralizer produces photolytic products, the photolytic products are of low or no toxicity to humans or animals.
- 23. The method of claim 1, wherein said microorganism neutralizer is:

24. The method of claim 1, wherein said microorganism neutralizer is:

- 25. A method for treating a fluid to neutralize microorganisms which may be present therein, said method comprising:
 - (a) adding to said fluid a neutralization-effective amount of a microorganism neutralizer of formula:

wherein R1, R2, R3, R4, R5 and R6 are, independently from one another, selected from the group consisting of hydrogen; -OH; -NH₂; -SO₄; -PO₄; -Cl; -Br; -I; optionally substituted alkyl, alkenyl, alkynyl or aryl groups with from 1 to 20 carbon atoms, said groups optionally substituted with one or more of -O-, -S-, -OH, -NH₂, -SO₄, -PO₄, -Cl, -Br, and -I; salts of the foregoing;

and -NR^a-(CR^bR^e)_n-X wherein X is a halogen selected from the group consisting of chlorine, bromine and iodine, R^a, R^b and R^e are, independently of each other, selected from the group consisting of hydrogen; optionally substituted alkyl, alkenyl, alkynyl and aryl groups with from 1 to 20 carbon atoms, said groups optionally substituted with one or more of -O-, -S-, -OH, -NH₂, -SO₄, -PO₄, -Cl, -Br, -I; and halogen selected from the

group -Cl, -Br, and -I; and n is an integer from 0 to 20; provided that R1 is not -OH or a straight chain alkyl group where the second carbon of the chain is substituted with -OH or =O except that the compound may be

or

and provided that R1, R4, R5 are not all methyl groups when R2, R3 and R6 are all hydrogen; and provided that the neutralizer is not:

wherein X is a halogen selected from the group consisting of chlorine, bromine and iodine, R^a, R^b and R^c are, independently of each other, selected from the group consisting of hydrogen, optionally substituted hydrocarbyl, and halogen selected from the group consisting of chlorine, bromine and iodine, and n is an integer from 0 to 20; and provided

that the compound is not:

wherein W is a water soluble group; and

- (b) exposing the fluid of step (a) to a triggering event whereby said microorganisms are neutralized.
- 26. The method of claim 25, wherein R1, R2, R3, R4, R5 and R6 are, independently from one another, selected from the group consisting of hydrogen; straight chain or cyclic saccharides having 5 or 6 carbon atoms; amino acid; -OH; -NH₂;-SO₄; -PO₄; -Cl; -Br; -I;

and optionally substituted alkyl, alkenyl, aryl and alkynyl groups with from 1 to 20 carbon atoms containing one or more members selected from the group consisting of: -O-, -C(=O), -C(=O)H, -C(=O)-OH, -OH, $-NH_2$, $-SO_4$, $-PO_4$, -Cl, -Br and -I.

- 27. The method of claim 25, wherein said fluid is a food product.
- 28. The method of claim 25, wherein said fluid is a drink meant for human or animal consumption.

- 29. The method of claim 25, wherein said fluid is a peritoneal dialysis solution.
- 30. A method of neutralizing microorganisms on a surface, comprising:
 - (a) applying to said surface an neutralization-effective amount of a compound of formula:

wherein R1, R2, R3, R4, R5 and R6 are, independently from one another, selected from the group consisting of hydrogen; -OH; NH_2 , -SO₄, -PO₄, -Cl, -Br, -I; straight chain or cyclic saccharides with 5 or 6 carbon atoms; amino acid groups;

$$\begin{array}{c|c} \text{OH} & \text{OH} \\ -\text{C} - \text{CH}_2\text{O} \\ \text{H} & \text{OH} \end{array}$$

optionally substituted alkyl, alkenyl, alkynyl or aryl groups with from 1 to 20 carbon atoms, said groups optionally substituted with one or more of -O-, -S-, -OH, -NH $_2$, -SO $_4$, -PO $_4$, -Cl, -Br, -I; salts of the foregoing;

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and -NR^a-(CR^bR^c)_n-X wherein X is a halogen selected from the group consisting of chlorine, bromine and iodine, R^a, R^b and R^c are, independently of each other, selected from the group consisting of hydrogen; straight chain or cyclic saccharides with 5 or 6 carbon atoms;

$$\begin{array}{c|c} OH \\ C \\ -CH_2O- \\ H \\ HO \end{array}$$

amino acid groups; optionally substituted alkyl, alkenyl, alkynyl or aryl groups with from 1 to 20 carbon atoms, said groups optionally substituted with one or more of -O-, -S-, -OH, -NH₂, -SO₄, -PO₄, -Cl, -Br, -I; and halogen selected from the group consisting of chlorine, bromine and iodine, and n is an integer from 0 to 20;

provided that R1 is neither H nor -OH nor a straight chain alkyl group where the second carbon of the chain is substituted with -OH or =O except that the compound may be

and provided that R1, R4, R5 are not all methyl groups when R2, R3 and R6 are all hydrogen; and provided that the neutralizer is not:

wherein X is a halogen selected from the group consisting of chlorine, bromine and iodine, R^a, R^b and R^c are, independently of each other, selected from the group consisting of hydrogen, optionally substituted hydrocarbyl, and halogen selected from the group consisting of chlorine, bromine and iodine, and n is an integer from 0 to 20; and provided that the compound is not:

wherein W is a water soluble group; and

- (b) exposing said surface to a triggering event whereby said microorganisms are neutralized
- The method of claim 30, wherein R1, R2, R3, R4, R5 and R6 are, independently from one another, selected from the group consisting of hydrogen; straight chain or cyclic saccharides with 5 or 6 carbon atoms; amino acid groups;-OH; -NH₂;-SO₄; -PO₄; -Cl; -Br; -I;

$$\begin{array}{c|c} \text{OH} \\ \text{C} - \text{CH}_2\text{O-} \\ \text{H} \\ \text{HO} & \text{OH} \end{array}$$

and alkyl, alkenyl, alkynyl or aryl groups with from 1 to 20 carbon atoms containing one or more members selected from the group consisting of: -O-, -C(=O), -C(=O)H, -C(=O)-OH,-Cl, -Br, -I, -OH, -NH₂, -SO₄, and -PO₄.

- 32. The method of claim 30, wherein said surface is a food surface.
- 33. The method of claim 30, wherein said surface is the surface of an animal carcass.
- 34. The method of claim 30, wherein said surface is a food-preparation surface.
- 35. The method of claim 30, wherein said surface is a surface of a bathing or washing vessel.
- 36. The method of claim 30, wherein said surface is a wound surface.
- 15 37. A fluid comprising biologically active protein, blood or blood constituents, and microorganism neutralizer, made by the method of claim 1.

- 38. A blood product comprising a microorganism neutralizer, made by the method of claim 1.
- 39. A non-toxic composition comprising a blood product additive photosensitizer for inactivating microorganisms suitable for administration to a patient having the structure:

$$\begin{array}{c|ccccc}
R_3 & R_1 \\
R_4 & N & N & O \\
R_5 & R_6 & O & R_2
\end{array}$$

wherein R1, R2, R3, R4, R5 and R6 are, independently from one another, selected from the group consisting of hydrogen; -OH; -NH₂; -SO₄; -PO₄; -Cl; -Br; -I; straight chain or cyclic saccharides with 5 or 6 carbon atoms;

amino acid groups; optionally substituted alkyl, alkenyl, alkynyl or aryl groups with from 1 to 20 carbon atoms said groups optionally substituted with one or more of -O-, -S-, -OH, -NH $_2$, -SO $_4$, -PO $_4$, -Cl, -Br, -I;

-NR^a-(CR^bR^c)_n-X wherein X is a halogen selected from the group consisting of chlorine, bromine and iodine, R^a, R^b and R^c are, independently of each other, selected from the group consisting of hydrogen; straight chain or cyclic saccharides with 5 or 6 carbon atoms;

amino acid groups; optionally substituted alkyl, alkenyl, alkynyl or aryl groups with from 1 to 20 carbon atoms optionally substituted with one or more of -O-, -S-, -OH, -NH $_2$, -SO $_4$, -PO $_4$, -Cl, -Br, -I; and halogen selected from the group consisting of chlorine, bromine and iodine; and salts of the foregoing wherein n is an integer from 0 to 20;

provided that R1 is neither H nor -OH nor a straight chain alkyl group where the second carbon of the chain is substituted with -OH or =O except that the compound may be

or

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and provided that R1, R4, R5 are not all methyl groups when R2, R3 and R6 are hydrogen and R1 is not a 2-, 3-, 4- or 5- carbon straight chain alkyl that terminates in -OH, -COH, or -H when R2, R3 and R6 are H, and R4 and R5 are CH₃₂provided that R1 is not -OH or a straight chain alkyl group where the second carbon of the chain is substituted with -OH or =O; and R1 is not a 2-, 3-, 4- or 5- carbon straight chain alkyl that terminates in -OH, -COH, or -H when R2, R3 and R6 are H, and R4 and R5 are CH₃; R1 is not - CH₂CH₂-(CHOH)₂-CH₃ or -CH₂CH₂-(CHOH)₂
-CH₂SO₄ or 1'-D-sorbityl or 1'-D-dulcityl or 1'-D-rhamnityl or 1'-D,L-glyceryl or -CH₂-O-C(O)-CH₃ or -CH₂-O-C(O)-CH₂CH₃ or 2', 3', 4', 5'-di-O-isopropyrideneriboflavin or 8-aminooctyl when R2, R3 and R6 are H and R4 and R5 are CH₃; R1 is not 1'-D-sorbityl or 1'-D-dulcityl when R4 and R5 are both chlorines and when R2, R3 and R6 are all hydrogens; R5 is not ethyl or chloro when R1 and R4 are methyl and R2, R3 and R6 are all hydrogens; R4 and R5 are not both methoxy or both tetramethylene when R1 is methyl and R2, R3 and R6 are all hydrogens; R2 is not -CH₂CH₂NH when R1, R4 and R5 are CH₃ and R3 and R6 are H; R2 is not



when R1, R4 and R5 are CH₃ and R3 and R6 are H; R5 is not chloro when R4 is methoxy and R1 is ethyl-2'N-pyrrolidino and R2, R3, and R6 are hydrogen; R1 is not N,N-dimethylaminopropyl or N,N-diethylaminoethyl when R5 is chloro or methyl and R2, R3, R4 and R6 are hydrogen; R3 is not -NH(CH₂CH₂)Cl when R6 is -NH2 and R1, R2, R4 and R5 are H; R1, R4, R5 are not all methyl groups when all of R2, R3 and R6 are hydrogens; R1, R4, R5 and R2 are not all methyl groups when R3 and R6 are hydrogens; R2 is not carboxymethyl when R1, R4 and R5 are methyl and R3 and R6 are hydrogen; R4 is not -NH2 when R1 and R5 are methyl and R2, R3 and R6 are all hydrogen; R1 is not a phenyl group when R4 and R5 are methyl and R2, R3 and R6 are all H; R1 is not methyl or N,N-dimethylaminoethyl when all of R2, R3, R4, R5 and R6

are hydrogen; R2, R4, R5 are not all methyl when R1 is acetoxyethyl and R3 and R6 are hydrogen; R5 is not methyl when R1 is N,N-diethylaminoethyl and R2, R3, R4 and R6 are all hydrogen; R4 and R5 are not both chlorine when R1 is methyl and R2, R3 and R6 are all hydrogen; R1 is not ethyl, β -chloroethyl, n-butyl, anilino, benzyl, phenyl, p-tolyl or p-anisyl when R5 is NH₂ and R2, R3, R4 and R6 are all hydrogen; and R4 is not chlorine when R1 is N,N-dimethylaminopropyl and R2, R3, R5 and R6 are all hydrogen;

provided that the compound is not:

wherein R is selected from the group consisting of hydrogen and optionally substituted straight chain or branched alkyl having from 1 to 20 carbon atoms; and provided that the compound is not:

wherein R is selected from the group consisting of hydrogen and optionally substituted straight chain or branched alkyl having from 1 to 20 carbon atoms; and provided that the compound is not:

wherein W is a water soluble group; and provided that R4 is not -OH, -Br, -Cl, -SH, -O-Alk, or -SAlk when R5 is CH3; R6, R3 and R2 are H and when R1 is Alk or H, where Alk is an alkyl chain of 1 to 4 carbon atoms; provided that R2 is not a 11 carbon straight chain alkyl group when R1, R3, R6 are H and R4 and R5 are methyl; and provided that R2 is not octadecyl or undecyl when R4 and R5 are methyl and R1, R3 and R6 are hydrogen; and provided that R2 is not a benzyl group when R1, R4 and R5 are methyl; and R3 and R6 are hydrogen; and provided that R1 or R2 do not contain a poly(pyrrolecarboxaminde) group; and provided that R5 is not bromo, chloro, nitro or trifluoromethyl when R2 is hydrogen, methyl, hydroxyethyl or benzyl and R3 and R6 are hydrogen and R1 is ethyl, propyl, isopropyl, butyl, pentyl, hexyl, phenyl, benzyl, phenehtyl, naphthyl, p-tolyl, p-ethylphenyl, p-anisyl, p-ethoxyphenyl, p-butoxyphenyl, 3,4-dicholorophenyl, methoxyethyl or ethoxyethyl; and provided that R1 is not a five carbon alkyl chain where four carbons are substituted with -O-COR where RCO is a straight chain alkanoyl group containing from 4 to 20 carbon atoms; and provided that R1 is not a phosphoric acid substituted hydroxyalkyl group when R2, R3, R4, R5 and R6 are hydrogen; and provided that R1 is not a two to six member alkyl chain terminated with a sulfate radical, a phosphate radical or an acyloxy radical, the acyl group of which is derived from an organic acid with not more than eighteen carbon atoms.

40. The compound of claim 39, wherein more than one of R1, R2, R3, R4, R5 and R6 are neither CH₃ nor H.

- 41. The compound of claim 40, wherein more than one of R2, R3, R4, R5 and R6 are neither H nor CH₃.
- 42. The compound of claim 40, wherein a R1, R2, R3, R4, R5 and R6 that is neither CH₃ nor H imparts substantial water solubility to the compound.
- 5 43. The compound of claim 42, wherein said R1, R2, R3, R4, R5 and R6 is selected from the group consisting of:

straight chain or cyclic saccharides with 5 or 6 carbon atoms;

and alkyl, alkenyl, alkynyl or aryl groups with 1 to 20 carbon atoms containing one or more members selected from the group consisting of: -O-, -OH, -NH₂, -SO₄, -PO₄.

- 44. The compound of claim 43, wherein R3 and R6 are H.
- 45. The compound of claim 40, wherein at least one of R1, R2, R3, R4, R5 and R6 contains a halogen selected from the group consisting of chlorine, bromine and iodine.
- 46. The compound of claim 45, wherein at least one of R1, R2, R3, R4, R5 and R6 is (CH₂)n-X, wherein n is either 1 or 2, and X is a halogen selected from the group consisting of chlorine, bromine and iodine.
- 47. The compound of claim 45, wherein at least one of the halogenated R1, R2, R3, R4, R5 and R6 is -NR(CH₂)n-X, wherein R is hydrogen or straight chain alkyl group consisting

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of one to 6 carbon atoms, n is an integer from 0 to 6, and X is selected from the group consisting of chlorine, bromine and iodine.

- 48. The compound of claim 45 wherein R4 or R5 is -NR(CH₂)n-X, wherein R is hydrogen or straight chain alkyl group consisting of one to 6 carbon atoms, n is an integer from 0 to 6, and X is selected from the group consisting of chlorine, bromine and iodine.
- 49. The compound of claim 39, wherein one of R1, R2, R3, R4, R5 and R6 is neither CH₃ nor H.
- 50. The compound of claim 49, wherein the R1, R2, R3, R4, R5 and R6 that is neither CH₃ nor H imparts substantial water solubility to the compound.
- 51. The compound of claim 50, wherein the R1, R2, R3, R4, R5 and R6 that imparts substantial water solubility to the compound is selected from the group consisting of: straight chain or cyclic saccharides having 5 or 6 carbon atoms; -OH; -NH₂; -SO₄; -PO₄;

and alkyl, alkenyl, alkynyl or aryl groups containing one or more members selected from the group consisting of: -OH, -O-, -S-, -NH $_2$, -SO $_4$, and -PO $_4$.

- 52. The compound of claim 51, wherein R2, R3, R4, R5 or R6 is neither H nor CH₃.
 - 53. The compound of claim 51, wherein R3 and R6 are H.

- 54. The compound of claim 49, wherein one of R1, R2, R3, R4, R5 and R6 is halogenated, wherein the halogen is selected from the group consisting of chlorine, bromine and iodine.
- 55. The compound of claim 54, wherein one of R1, R2, R3, R4, R5 and R6 is -(CH₂)n-X, wherein n is either 1 or 2, X is a halogen selected from the group consisting of chlorine, bromine and iodine.
- 56. The compound of claim 54, wherein one of R1, R2, R3, R4, R5 and R6 is -NR(CH₂)n-X, wherein R is hydrogen or straight chain alkyl group consisting of one to 6 carbon atoms, n is an integer from 0 to 6, and X is selected from the group consisting of chlorine, bromine and iodine.
- 57. The compound of claim 56 wherein R4 or R5 is -NR(CH₂)n-X, wherein R is hydrogen or straight chain alkyl group consisting of one to 6 carbon atoms, n is an integer from 0 to 6, and X is selected from the group consisting of chlorine, bromine and iodine.
- 58. The compound of claim 39 wherein at least one of R1, R2, R3, R4, R5 and R6 are branched or unbranched alkyl groups having 1 to 20 carbon atoms substituted with at least one -OH group.

59. The compound of claim 39 having the structure:

wherein R is selected from the group consisting of: straight chain or cyclic saccharides having 5 or 6 carbon atoms; -OH-; -NH₂; -SO₄; -PO₄; and alkyl, alkenyl, alkynyl or aryl groups having from 1 to 20 carbon atoms containing one or more members selected from the group consisting of: -O-; -OH-; -NH₂; -SO₄; and -PO₄.

- 60. The compound of claim 39 wherein at least one of R1, R2, R3, R4, R5 and R6 are alkylating agents.
- 61. The compound of claim 39 wherein at least one of R1, R2, R3, R4, R5 and R6 are substituents that cause the compound to be substantially nonreactive to microorganisms at substantially neutral pH and active toward microorganism neutralization at the pH of the biological fluid.
- 62. The compound of claim 39 having the structure:

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63. The compound of claim 39 having the structure: